201-16128

Lisa Medley/DC/USEPA/US
12/29/2005 09:40 AM

To NCIC HPV@EPA
cc
bcc
Subject Fw: Diene 221 (CAS #2611-00-9) HPV submission part 1

Lisa Medley
OPPT/OSWER Docket - EPA HQ Docket Center
(Operated by ASRC Management Services)
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----- Forwarded by Lisa Medley/DC/USEPA/US on 12/29/2005 09:40 AM -----

"Nitschke, Kenneth (KD)"
<kdnitsch@dow.com>
12/29/2005 08:39 AM

To NCIC OPPT@EPA, Rtk Chem@EPA
cc
Subject Diene 221 (CAS #2611-00-9) HPV submission part 1

Dear Sir - Enclosed is a cover letter, Test Plan and Dossier for 3-Cyclohexene-1-carboxylic acid, 3-cyclohexen-1-ylmethyl ester (Diene 221) (CAS #2611-00-9). As mentioned in the cover letter, I will also resubmit the dossier on Tetrahydrobenzaldehyde (CAS#100-50-5) in a separate e-mail. Thank you.

Ken
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<<Diene 221 cover leter.pdf>> <<Diene 221 Dossier.pdf>> <<Diene 221 Test Plan .pdf>> <<Diene 221 Test Plan Tables.pdf>>

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201-16128

The Dow Chemical Company
Midland, Michigan 48674

22 December 2005

Mr Michael O. Leavitt, Administrator
US Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116

Attention: Chemical Right-to-Know Program

On behalf of The Dow Chemical Company, I am submiting the test plan and robust summaries in IUCLID format for 3-Cyclohexene-1-carboxylic acid, 3-cyclohexen-1-ylmethyl ester (Diene 221) (CAS NO. 2611-00-9). Since this material is expected to degrade to Tetrahydrobenzaldehyde (CAS NO. 100-50-5), I have also enclosed the robust summaries previously submitted for it. All documents are in Adobe Acrobat (pdf) files.

We understand this information will be posted on the internet for comments for a period of 120 days. Please forward comments to me at the address below.

Sincerely,

Kenneth D. Nitschke, D.A.B.T
The Dow Chemical Company
1803 Bldg.
Midland, MI 48674

201-16128

HIGH PRODUCTION VOLUME (HPV)

CHEMICALS CHALLENGE PROGRAM

TEST PLAN

For

3-Cyclohexene-1-carboxylic acid, 3-cyclohexen-1-ylmethyl ester (Diene 221)

CAS NO. 2611-00-9

December 2005

Prepared by:

The Dow Chemical Company
Midland, Michigan 48674

EXECUTE SUMMARY

The Dow Chemical Company voluntarily submits the following screening information data and Test Plan covering the chemical 3-cyclohexene-1-carboxylic acid, 3-cyclohexen-1-ylmethyl ester, also known as Diene 221 (CAS No. 2611-00-9), for review under the Environmental Protection Agency's High Production Volume (HPV) Chemicals Challenge Program. Since this material is produced in a closed system at one site and as an intermediate is rapidly reacted to produce the final product, a limited amount of physical chemical and mammalian toxicity data exists to evaluate the potential hazards associated with Diene 221. Two moles of tetrahydrobenzaldehyde (THBA) are reacted to produce a mole of Diene 221. Peracetic acid is subsequently reacted with Diene 221 to produce the final product. Available data for the Diene 221 precursor, THBA, which is expected to be metabolized to the same degradation product as Diene 221, tetrahydrobenzoic acid, is presented. Thus, the information on THBA is expected to serve as a surrogate for Diene 221. Both THBA and peracetic acid are corrosive materials. Since Diene 221 is a closed system intermediate there is no need for a reproduction study. Based on the limited number of workers exposed to this material, the corrosive nature of THBA and peracetic acid which have resulted in a high degree of personal protective equipment whenever exposure is possible, the available data on THBA is considered sufficient to address the biodegradation and environmental and mammalian toxicology HPV endpoints. However, the HPV physical chemical endpoints will be measured and the fugacity models recalculated.

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TEST PLAN FOR
3-Cyclohexene-1-carboxylic acid, 3-cyclohexen-1-ylmethyl ester (Diene 221)

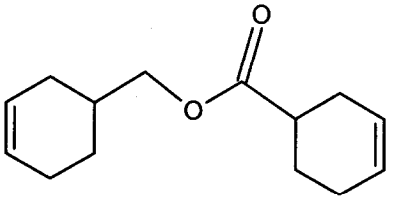
CAS Nos. 2611-00-9

I. INTRODUCTION AND IDENTIFICATION OF CHEMICAL

Under EPA's High Production Volume (HPV) Chemicals Challenge Program, The Dow Chemical Company (Dow) has committed to voluntarily compile basic screening data on 3-cyclohexene-1-carboxylic acid, 3-cyclohexen-1-ylmethyl ester (Diene 221). The data included in this Test Plan include physicochemical properties, environmental fate, and human and environmental effects of Diene 221, as defined by the Organization for Economic Cooperation and Development (OECD). Because Diene 221 is an ester, esterases as well as alcohol and aldehyde dehydrogenases present in microorganisms, aquatic species and mammals should rapidly degrade Diene 221 and tetrahydrobenzaldehyde (THBA) to the same degradation product. Thus information on THBA, also part of the EPA's HPV program, is also provided. The information provided comes from existing data developed by or on behalf of Dow, or is found in the published scientific literature.

A. Structure and Nomenclature

Following is a structural characterization of Diene 221 and its associated nomenclature.



Diene 221

B. Manufacturing & Use

Union Carbide Corporation, a subsidiary of The Dow Chemical Company, operates a single manufacturing site producing Diene 221. Two moles of THBA are reacted to produce a mole of Diene 221 which is subsequently reacted with peracetic acid to produce the final product.

THBA has an odor threshold of approximately 0.22 ppm, and will be detected by smell before air concentrations reach unsafe levels.

Approximately 50 individuals are involved in the manufacture or use of THBA and these individuals have extremely low potential for skin and airborne exposure. Due to the subacute hazards associated with exposure to THBA, an occupational exposure limit of 5 ppm (Union Carbide Occupational Exposure Guideline) has been set. This has resulted in specific manufacturing procedures and practices to minimize the exposure potential to THBA. Between 1988 and 1998, over 300 samples were obtained

from the THBA production and use plants. Only two values were greater than 1 ppm, and both of these were below the UCC Occupational Exposure Guideline. A review of more recent industrial hygiene samples from 1999 to the present in both manufacturing and use facilities have also shown that all samples are 1 ppm or lower. Due to the corrosive nature of THBA, personal protective equipment including (self-contained breathing apparatus (SCBA) when vapor exposure is high (considered to be greater than the action level (2.5 ppm) of the UCC Occupational Exposure Guideline), monogoggles, gloves and chemical apron, are worn whenever exposure to THBA is possible. Such operations could include sampling and material transfer operations, shutdown and clean-up activities.

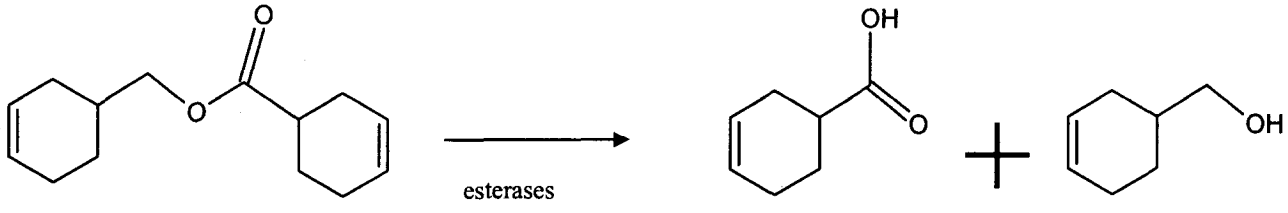
Following the production of Diene 221, the material undergoes another chemical reaction with peracetic acid to produce the final product. Roughly the same number of individuals work in this plant as in the THBA plant. The amount of Diene 221 present in the final product is expected to be very low, probably less than 1 ppm.

Peracetic acid, C_2O_3, has an odor threshold estimated to be 50 ppb (Ancker and Zetterberg, 1997). Peracetic acid has a pungent, vinegar-like odor (Swern, 1970). Concentrations of 150 ppb are considered tolerable and not unpleasant to humans while 350 ppb are considered unpleasant when inhaled for long time periods (McDonagh, 1997). Typical concentrations of peracetic acid measured outside of the reactor are below the detection limit of 20 ppb. During maintenance, concentrations of <1 ppm peracetic acid have been measured. Since peracetic acid is corrosive to the skin and eyes, protective equipment required during maintenance includes full-face respirator, air-purifying or positive-pressure supplied-air respirator, and full chemical resistant suit depending on operation.

Due to the corrosive nature of both THBA and peracetic acid, the personal protective equipment worn to prevent exposure to either of these chemicals will also protect workers from exposure to Diene 221. Since Diene 221 is less volatile than either THBA or peracetic acid, exposure to Diene 221 should be well below the measured values for THBA or peracetic acid. Since Diene 221 is produced and reacted in a closed system, release to the environment is expected to be quite rare.

II. METABOLISM.

Uptake of Diene 221 by microorganisms, aquatic species or mammals is expected to result in quite rapid metabolism by esterases resulting in formation of tetrahydrobenzoic acid and tetrahydrobenzyl alcohol. The tetrahydrobenzyl alcohol is expected to be rapidly metabolized to the aldehyde, tetrahydrobenzaldehyde (THBA), the precursor for Diene 221. THBA will be rapidly metabolized to the acid. The two enzymes forming the aldehyde and the acid are alcohol dehydrogenase and aldehyde dehydrogenase. These reactions are expected to occur relatively rapidly. Therefore available toxicity data for THBA should be relevant and acceptable for Diene 221 and tetrahydrobenzoic acid.

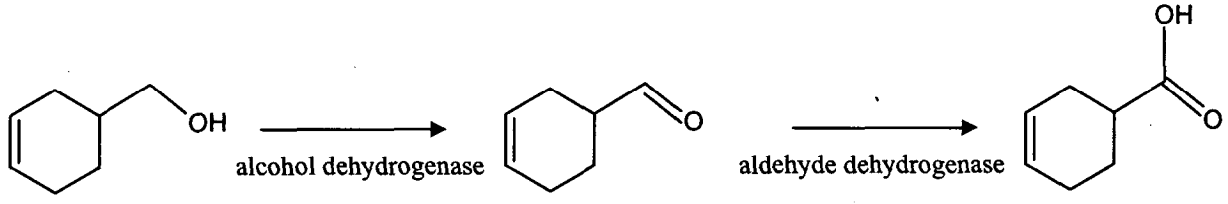


Diene 221
Tetrahydrobenzyl

Tetrahydrobenzoic

Acid

Alcohol



Tetrahydrobenzyl
Alcohol

Tetrahydrobenzaldehyde

Tetrahydrobenzoic
Acid

III. TEST PLAN RATIONALE

The information included in this Test Plan has come from one or more of the following sources:
1) Internal studies conducted by or on behalf of The Dow Chemical Company
2) Studies that have been extracted from the scientific literature either as primary references, or as reported in well-accepted, peer-reviewed reference books
3) Calculation methods or quantitative structure-activity relationships (QSAR) which are accepted by the US EPA for such purposes (1999b).

This assessment includes information on physicochemical properties, environmental fate, and human and environmental effects associated with Diene 221. Information is also provided for THBA since Diene 221 is expected to be metabolized to tetrahydrobenzoic acid in either aquatic or mammalian organisms. The data used to support this program include those Endpoints identified by the US EPA (1998). Key studies have been identified for each data Endpoint, and are summarized in Robust Summary form in Section VII of this Dossier.

All studies were reviewed and assessed for reliability according to standards specified by Klimisch *et al* (1997), as recommended by the US EPA (1999a). The following criteria were used for codification:
1. Valid without Restriction - Includes studies which comply with US EPA and/or OECD-accepted testing guidelines, which were conducted using Good Laboratory Practices (GLPs) and for which test parameters are complete and well documented,
2. Valid with Restrictions – Includes studies which were conducted according to national/international testing guidance and are well documented. May include studies conducted prior to establishment of testing standards or GLPs but meet the test parameters and data documentation of subsequent guidance;

also includes studies with test parameters which are well documented and scientifically valid but vary slightly from current testing guidance. Also included are physical-chemical property data obtained from reference handbooks as well as environmental endpoint values obtained from an accepted method of estimation (i.e. EPIWIN).
3. Not Valid – Includes studies in which there are interferences in either the study design or results that provide scientific uncertainty or where documentation is insufficient.
4. Not Assignable – Includes studies in which limited data is provided.

Those studies receiving a Klimisch rating of 1 or 2 are considered adequate to support data assessment needs in this Test Plan.

IV. TEST PLAN SUMMARY AND CONCLUSIONS

Physical-chemical property values (Melting Point, Boiling Point, Vapor Pressure, Partition Coefficient and Water Solubility) were calculated. We know the melting point is lower than the estimated value of 46.9°C since it is a liquid at room temperature, 25°C. Therefore, we will repeat the physical property measurements as regards melting point, boiling point, vapor pressure, water solubility and Kow. The partition coefficient, log Kow, is approximately 5. Although the log Kow is estimated to be nearly 5, the activity of esterases upon Diene 221 will increase the water solubility of the resultant products.

Environmental Fate values for Hydrolysis, Photodegradation, and Transport (Fugacity) were obtained using computer estimation –modeling programs. The model predicts Diene 221 will slowly hydrolyze. The fugacity model level 3 predicts that most of the material emitted will end up in soil (65%) with 15.6% in water and 19% in sediment. A very small amount will remain in air. Any material that is released to the air will be rapidly photodegraded via reaction with hydroxyl radical and ozone. The AopWin predicted half life in the atmosphere is approximately 41 minutes (0.7 hr.). Four of the 6 biodegradation computer estimation-modeling programs (Biowin (v4.02) predict the material will biodegrade rapidly. The primary biodegradation timeframe is predicted to be days while the ultimate biodegradation timeframe is weeks. Thus all of the models predict Diene 221 will degrade quite rapidly. Esterases are expected to degrade Diene 221 to the acid and the alcohol. The alcohol will be rapidly degraded to the aldehyde and then to the acid. The aldehyde, THBA, was shown to be readily biodegradable, using a test procedure which was equivalent to OECD Test Guideline 301D. Thus models and available data on structurally similar material indicate Diene 221 will be degraded very rapidly.

Ecotoxicity values for Diene 221 have been estimated for fish, daphnia and algae. The estimated values range from 0.08 mg/L in algae to 0.86 mg/L in fish. Since aquatic organisms have esterase enzymes Diene 221 should be rapidly metabolized to tetrahydrobenzoic acid and tetrahydrobenzyl alcohol. The alcohol should be further metabolized to the aldehyde and then to the acid. Thus the available data for THBA should be representative for Diene 221 also and would predict much higher LC50 and EC50 values than has been estimated for Diene 221.

Mammalian Toxicity endpoints are limited to acute parameters. The material causes minor irritation in dermal and eye irritation studies. The dermal LD50 value is $\geq$12325 mg/kg while the oral LD50 ranges from 1363 mg/kg in females to 2386 mg/kg in males. The lowest oral LD50 value is approximately half that of THBA which supports the premise that Diene 221 and THBA are rapidly metabolized to common degradation products.

Although no repeated dose, mutagenicity or developmental toxicity data is available, several two week studies have been conducted on THBA via two different routes. As part of these studies, the testes and ovaries were weighed and testes examined histopathologically. However, for reproductive toxicity purposes, these studies were of short duration and therefore rated a 4 in the Klimisch rating system. Although the study was of a short duration, there were no significant treatment-related effects noted which would indicate a reproductive effect. No developmental toxicity study was found. Point mutation and chromosomal aberration assays of THBA were negative. Given that Diene 221 and THBA are expected to be metabolized to common degradation products and given that Diene 221 is used as a closed system intermediate and exposure will be limited due to the corrosive nature of other chemicals used in it's manufacture, additional toxicity studies are considered unnecessary.

A tabular depiction of data availability and testing recommendations for Diene 221 can be found in Table 1.

V. DATA SET SUMMARY AND EVALUATION

The key studies used in this assessment to fulfill the HPV requirements have been placed in an Endpoint-specific matrix, and are further discussed below. Robust Summaries for each study referenced can be found in Section VII of this dossier.

A. Chemical/Physical Properties

All HPV Endpoints for Chemical/Physical Properties have been calculated for Diene 221 (Table 2). Additional information is provided from the THBA test plan. The melting point is estimated to be 47°C, indicating Diene 221 is a solid at room temperature. However, the material is a liquid at room temperature. We will repeat the physical property measurements as regards melting point, boiling point, vapor pressure, water solubility and Kow.

B. Environmental Fate and Biodegradation

All HPV Endpoints for Environmental Fate have been calculated for Diene 221 (Table 3). Additional information is provided from the THBA test plan. Based on the presence of esterases and alcohol and aldehyde dehydrogenases in microorganisms, Diene 221 and THBA are expected to be rapidly degraded to tetrahydrobenzoic acid. THBA has been reported to be readily biodegradable in an OECD 301D test. The Fugacity Model will be recalculated with actual physical chemical values.

C. Aquatic Toxicity

Aquatic toxicity data has been calculated for fish, daphnia and algae for Diene 221 (Table 4). Calculated acute ecotoxicity values were estimated using the esters class in the ECOSAR v0.99h program. Additional information is provided from the THBA test plan. Based on the presence of esterases and alcohol and aldehyde dehydrogenases in all aquatic genera used for toxicity testing, we would expect the LC50 or EC50 values to be approximately half the value for THBA. The Diene 221values are predicted to be half of the THBA value, since two moles of THBA are produced for each mole of Diene 221.

D. Mammalian Toxicity Endpoints

Summaries of available toxicity data used to fulfill the HPV Endpoints for Mammalian Toxicity are found in Tables 5-7. Each of the Key Studies has been further summarized in the Robust Summary section of this Dossier. Additional information is provided from the THBA test plan.

1.0 Acute Toxicity

The acute oral LD_{50} values are 1363 mg/kg and 2386 mg/kg in female and male rats, respectively. The acute dermal LD50 is $\geq$12,325 mg/kg. A saturated atmosphere did not produce lethality. Diene 221 produced minor erythema to the skin and minor conjunctival irritation. There was no evidence of corneal damage. Based on the presence of esterases and alcohol and aldehyde dehydrogenases in all mammals, Diene 221 and THBA are expected to be metabolized to common degradation products. There appears to be reasonably good agreement between the Diene 221 oral LD50 value for rats with that of THBA. Given that Diene 221 produces only minor irritation to the skin and the larger MW of this material, the dermal LD50 is much greater than for THBA which is a corrosive material.

2.0 Repeated Dose Toxicity

There is no repeated dose toxicity data for Diene 221. However, two separate two-week inhalation toxicity studies, as well as a two-week dermal toxicity study have been conducted with THBA (Table 6). Doses causing severe irritation at the application site in the dermal study produced only slight effects (mineral deposits) in the kidney. Inhalation exposure to THBA resulted in histopathologic changes in the nasal tissues. In these same animals, clinical changes in kidney function were observed, which included decreases in urine volume, pH and osmolality. However, there was no evidence of histopathologic changes. Thus, following the two most likely routes of exposure for humans, only minimal changes were observed at levels which resulted in severe irritation at the portal of entry.

3.0 Developmental Toxicity

There is no available developmental toxicity study (Table 6). However due to the corrosive nature of the precursors used to manufacture Diene 221 or subsequently reacted with Diene 221 an increased level of personal protective equipment is required. Given the limited number of individuals exposed to Diene 221 and the low concentrations of THBA or peracetic acid measured in the workplace, a developmental toxicity study of Diene 221 is considered to be unnecessary.

4.0 Reproductive Toxicity

There is no available reproduction toxicity study (Table 6). Several two week studies have been conducted via two different routes of THBA. As part of these studies, the testes and ovaries were weighed and testes examined histopathologically. However, for reproductive toxicity purposes, these studies were of short duration and therefore rated a 4 in the Klimisch rating system. Although the study was of a short duration and produced severe irritation at the dermal application site and slight effects in the kidney, there were no significant treatment-related effects noted which would indicate a reproductive effect. Since the material is used solely as a chemical intermediate with limited worker exposure, a reproductive toxicity study is considered unnecessary.

5.0 Mutagenicity and Chromosomal Aberrations

5.1 Mutagenicity Testing (Ames test)
There is no available data on Diene 221. THBA was negative in the Ames test.

5.2 - Chromosomal Aberrations
There is no available data on Diene 221. THBA was negative in the in vitro CHO/HGPRT assay and in the in vivo mouse micronucleus assay.

If we are unable to document the physical chemical properties cited on the MSDS, the following physical chemical measurements will be conducted: melting point, boiling point, vapor pressure, water solubility and Kow. The Fugacity Model will be recalculated with actual physical chemical values. Although there is no toxicity data for Diene 221, it is expected to rapidly be degraded by esterases and alcohol and aldehyde dehydrogenases to tetrahydrobenzoic acid. Since it is a closed system intermediate with a minimal number of individuals who are required to wear protective gear to reduce exposure to other chemicals in the workplace, no additional toxicity studies are necessary.

VI. REFERENCES

ACGIH TLV (2002). Threshold Limit Values for chemical substances and physical agents and Biological Exposure Indices. American Conference of Governmental Industrial Hygienists.

Ancker, K. and Zetterberg, L. (1997). Measurement of peracetic acid at Eka Chemicals AB, Bohus. Unpublished report A97329 for Eka Chemicals. Cited in ECETOC (2001). Peracetic acid (Cas No. 79-21-0) and its equilibrium solutions. JACC # 40.

Klimisch, H.-J., Andreae, M. and Tillman, U. (1997). A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data. Regul. Toxicol. Pharmacol. 25:1-5.

McDonagh, J. (1997). Atmospheric monitoring of peracetic acid on the existing caprolactone plant distillation houses A&B, assessment of results. Personal communication from Solvay Interox, Warrington. Cited in ECETOC (2001). Peracetic acid (Cas No. 79-21-0) and its equilibrium solutions. JACC # 40.

Swern, D. (1970). Organic peroxides Vol 1. Wiley Interscience, New York, NY, USA, pp340-369, 461-474 Cited in ECETOC (2001). Peracetic acid (Cas No. 79-21-0) and its equilibrium solutions. JACC # 40.

US EPA, (1998). Guidance for meeting the SIDS requirements (The SIDS Guide). Guidance for the HPV Challenge Program (11/31/98).

US EPA, (1999a). Determining the adequacy of existing data. Guidance for the HPV Challenge Program (2/10/99).

US EPA, (1999b). The use of structure-activity relationships (SAR) in the High Production Volume Chemicals Challenge Program. OPPT, EPA.

VI. ROBUST STUDY SUMMARIES -IUCLID

Data Sets are appended

Table 1. Test Plan Matrix for Diene 221

	Info available?	OECD?	GLP?	Other study based on THBA	Estimated method?	Acceptable?	Testing recommendation?
PHYSICAL CHEMICAL							
Melting Point	Y	N	N	N	Y	Y, 2	Y
Boiling Point	Y	N	N	N	Y	Y, 2	Y
Vapor Pressure	Y	N	N	N	Y	Y, 2	Y
Partition Coefficent	Y	N	N	N	Y	Y, 2	Y
Water Solubility	Y	N	N	N	Y	Y, 2	Y
ENVIRONMENTAL FATE ENDPOINTS							
Photodegradation	Y	N	N	N	Y	Y, 2	N
Biodegradation	Y	N	N	Y	Y	Y, 2	N
Hydrolysis	Y	N	N	N	Y	Y, 2	N
Transport between Environmental Compartmenats (Fugacity)	Y	N	N	N	Y	Y, 2	Y
Bioaccumulation	N	N	N	N	N	N	N
ECOTOXICITY							
Acute Toxicity to Fish	Y	N	N	Y	Y	Y, 2	N
Acute Toxicity to Aquatic Invertebrates	Y	N	N	Y	Y	Y, 2	N
Acute Toxicity to Aquatic Plants	Y	N	N	N	Y	Y, 2	N
MAMMALIAN TOXICITY							
Acute Toxicity	Y	Y	Y	Y	N	Y, 1A	N
Repeated Dose Toxicity	Y	N	N	Y	N	Y, 2	N
Genetic Toxicity - Mutation (Ames)	Y	N	N	Y	N	Y, 2	N
Genetic Toxicity - Chromosomal Aberrations	Y	N	N	Y	N	Y, 2	N
Developmental Toxicity	N	N	N	N	N	N	N
Reproductive Toxicity	N	N	N	N	N	N	N

Y = Yes; N = No; ND = No Data; S = Supplemental, not required under HPV; - = Not applicable

Table 2. Matrix of Available and Adequate Data on Diene 221
Physicochemical Properties

Name (CAS No.)	Melting Point (°C)	Vapor Pressure (hPa @ 25°C)	Boiling Point (°C)	Partition Coefficient (log Kow)	Water Solubility (mg/L @ 20C)
Diene 221 (2611-00-9)	46.9 (calculated)	0.00175 (calculated)	299 (calculated)	4.97 (calculated)	1.94 (calculated)
TETRAHYDROBENZALDEHYDE (THBA) (100-50-5)	-96.1 (measured)	2.97 (2.225 mm Hg) (calculated)	164 (measured)	1.89 (preferred calc.) 1.34 (other calc.)	0.5% Slightly soluble (measured)

Table 3. Matrix of Available and Adequate Data on Diene 221
Environmental Fate

Name (CAS No.)	**Hydrolysis**	**Photodegradation** Half life	**Biodegradation**	**Environmental Transport** Level III 1000 kg/hr released to air, water and soil
Diene 221 (2611-00-9)	Half life 9.2 years at 25C and pH 7 (calculated)	Hydroxyl Radicals Reaction: 126.5794 E-12 Ozone Reaction: 40.000000 E-17 cm3/molecule-sec Overall half life = 41 minutes (calculated)	Predicted to biodegrade rapidly (calculated)	Air 0.1% Water 15.6% Soil 65.3% Sediment 19%
Tetrahydrobenzadehyde (THBA) (100-50-5)	Not estimatable (Hyrowin 1.67) Does not contain hydrolyzable groups	Hydroxyl Radicals Reaction: 88.6330 E-12 Ozone Reaction: 20.000000 E-17 cm3/molecule-sec Overall half life = 0.7 hours (~42 minutes) (calculated)	readily biodegradable 76% in a closed bottle test equivalent to OECD 301D	Air 0.035% Water 99.9% Soil 0.0033% Sediment 0.074%

Table 4. Matrix of Available and Adequate Data on Diene 221
Ecotoxicity

Name (CAS No.)	Acute Fish 96-hour LC50 (mg/l)	Acute Invertebrate 48-hour EC50 (mg/l)	Algal 72-hour growth inhibition EC50 (mg/l)
Diene 221 (2611-00-9)	~0.859 (estimated)	~0.347 (estimated)	~0.076 (estimated)
Tetrahydrobenzadehyde (THBA) (100-50-5)	No data for acute study Predicted 96 hr LC50 9.997 mg/L Chronic 14-day LC50 is 1.1 mg/L Predicted 32-day Chronic Value (ChV) is 0.885 mg/L	130 Predicted 48 hr LC50 6.85 mg/L	No data for acute study Predicted 96 hr EC50 68.4 mg/L

Table 5. Matrix of Available and Adequate Data on Diene 221
Acute Toxicity

Name (CAS No.)	Acute Oral	Acute Inhalation	Acute Dermal	Dermal Irritation	Eye Irritation	Sensitization
Diene 221 (2611-00-9)	1363 mg/kg females 2386 mg/kg males (measured)	> saturated atmosphere	≥12,325 mg/kg	Minor erythema	Minor conjunctival irritation	No Data
Tetrahydrobenzadehyde (THBA) (100-50-5)	2385 mg/kg	>1679 ppm for 6 hour exposure	1716mg/kg	Corrosive according to DOT test	Moderately severe corneal injury using 0.005 ml test material	No data

Table 6. Matrix of Available and Adequate Data on Diene 221
Repeat-dose Toxicity

Name (CAS No.)	Repeat Dose	Reproductive	Developmental
Diene 221 (2611-00-9)	No Data	No Data	No Data
Tetrahydrobenzadehyde (THBA) (100-50-5)	Two week inhalation NOEL – 5 ppm Two week dermal systemic NOEL – 0.10 ml/kg/day	No effect on ovary or testicular weights or testes histopath in two week dermal study	No data

Table 7. Matrix of Available and Adequate Data on Diene 221
Genotoxicity

Name (CAS No.)	Genotoxicity (*in vitro* -bacterial)	Genotoxicity (*in vitro* - mammalian)	Genotoxicity (*in vivo*)
Diene 221 (2611-00-9)	No Data	No Data	No Data
Tetrahydrobenzadehyde (THBA) (100-50-5)	Negative	Negative in CHO/HGPRT assay	Negative in mouse micronucleus assay

Table 8
Test Plan Matrix for Diene 221

	Diene 221 (2611-00-9)	Tetrahydrobenzaldehyde (THBA) (100-50-5)
Melting point, °C	-66 A	-96.1 (measured) A
Boiling point, °C	276 A	164 (measured) A
Vapor Pressure, hPa at 25°C	0.00175 (calculated) A	2.97 (calculated) A
Water Solubility , mg/L @20°C	1.94 (calculated) A	0.5% (measured) Slightly soluble A
K_{ow}	4.97 (calculated) A	1.89(calculated) A
Biodegradation	Predicted to readily degrade A	76% in closed bottle test equivalent to OECD 301D readily biodegradable A
Hydrolysis, half life at 20°C and pH 7	Does not contain hydrolysable groups A	Does not contain hydrolysable groups A
Photodegradability	Overall half life = 41 minutes A	Overall half life = 0.7 hours A
Transport between Environmental Compartments: **(Fugacity Level III Model)** Default assumption: 1000 kg/hr released into air, water, and soil.	Air 0.1% Water 15.6% Soil 65.3% Sediment 19% A	Air 0.035% Water 99.9% Soil 0.0033% Sediment 0.074% A
Acute Toxicity to Fish (96hr LC50)	~0.859mg/L (calculated) A	14-day is 1.1 mg/L (measured) A
Acute Toxicity to Aquatic Invertebrates (48hr EC50)	~0.347 mg/L (calculated) A	130 (measured) A
Toxicity to Aquatic Plants (72hr EC50)	~0.076 mg/L (calculated) A	68.4 (calculated)
Acute Toxicity (oral), mg/kg	≥1363 mg/kg A	2385 mg/kg A
Acute Toxicity (dermal) ml/kg	≥12,325 mg/kg	1716 mg/kg A
Acute Eye Irritation	Minor conjunctival irritation	Moderately severe corneal injury

	A	using 0.005 ml test material A
Acute Skin Irritation	Minor erythema A	Corrosive according to DOT test A
Repeated Dose Toxicity	No data R	Two week NOEL – 5 ppm A
Genetic Toxicity-Mutation	No data R	Negative A
Genetic Toxicity- Chromosomal Aberrations	No data R	Negative (in vitro) Negative (in vivo) A
Toxicity to Reproduction	No data NR	No data NR
Developmental Toxicity	No data NA	No data NA

Legend	
Symbol	**Description**
R	Endpoint requirement fulfilled using category approach, SAR
Test	Endpoint requirements to be fulfilled with testing
Calc	Endpoint requirement fulfilled based on calculated data
A	Endpoint requirement fulfilled with adequate existing data
NR	Not required per the OECD SIDS guidance
NA	Not applicable due to physical/chemical properties

201-16128

IUCLID

Data Set

Existing Chemical	:	ID: 2611-00-9
CAS No.	:	2611-00-9
EINECS Name	:	cyclohex-3-enylmethyl cyclohex-3-enecarboxylate
EC No.	:	220-031-5
Molecular Formula	:	C14H20O2
Producer related part		
Company	:	The Dow Chemical Company
Creation date	:	01.12.0005
Substance related part		
Company	:	The Dow Chemical Company
Creation date	:	01.12.0005
Status	:	
Memo	:	
Printing date	:	20.12.2005
Revision date	:	
Date of last update	:	20.12.2005
Number of pages	:	27
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1. General Information

Id 2611-00-9
Date 20.12.2005

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	manufacturer
Name	:	Dow Chemical
Contact person	:	
Date	:	01.12.2005
Street	:	
Town	:	48674 Midland, MI
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

05.12.2005

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

Type	:	manufacturer
Name of plant	:	
Street	:	
Town	:	
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

01.12.2005

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	
Smiles Code	:	O=C(OCC(CCC=C1)C1)C(CCC=C2)C2
Molecular formula	:	C14 H20 O2
Molecular weight	:	220.31
Petrol class	:	

09.12.2005

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	typical for marketed substance

Substance type	:	organic
Physical status	:	liquid
Purity	:	
Colour	:	Transparent colorless
Odour	:	Sweet

01.12.2005

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

3-Cyclohexene-1-Carboxylic Acid, 3-Cyclohexen-1-ylmethyl ester

05.12.2005

3-Cyclohexenyl 3-Cyclohexene 1-Carboxylate

05.12.2005

Diene 221

05.12.2005

1.3 IMPURITIES

Purity	:	typical for marketed substance
CAS-No	:	
EC-No	:	
EINECS-Name	:	4-(hydroxymethyl)1-cyclohexene
Molecular formula	:	
Value	:	<= 1 % v/v

20.12.2005

Purity	:	typical for marketed substance
CAS-No	:	100-50-5
EC-No	:	202-858-3
EINECS-Name	:	cyclohex-3-ene-1-carbaldehyde
Molecular formula	:	C7 H10 O1
Value	:	<= .3 % v/v

16.12.2005

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use	:	industrial
Category	:	Chemical industry: used in synthesis
Remark	:	Intermediate closed system
15.12.2005		

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

Source of exposure	:	other: Closed system intermediate - exposure is negligible
Exposure to the	:	

01.12.2005

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value	:	= 47 °C
Sublimation	:	
Method	:	other: calculated MPBPVP
Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4

19.12.2005 (1)

2.2 BOILING POINT

2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	= .001746523 hPa at 25 °C
Decomposition	:	
Method	:	other (calculated):MPBPWin
Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4

19.12.2005 (2)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	octanol-water
Log pow	:	ca. 4.97 at °C
pH value	:	
Method	:	other (calculated):KOWWIN
Year	:	
GLP	:	
Test substance	:	

19.12.2005 (2)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	= 1.94 mg/l at 25 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	

Stable	:	
Deg. product	:	
Method	:	other:WSKOWWIN
Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4

19.12.2005 (2)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	other:calculated
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
DIRECT PHOTOLYSIS		
Halflife t1/2	:	= .1 day(s)
Degradation	:	% after
Quantum yield	:	
INDIRECT PHOTOLYSIS		
Sensitizer	:	O3
Conc. of sensitizer	:	
Rate constant	:	= cm^3/(molecule*sec)
Degradation	:	% after
Deg. product	:	
Method	:	other (calculated)
Year	:	
GLP	:	
Test substance	:	

Remark : The fact that Diene 221 absorbs light in the >290 nm wavelength range merely indicates that photodecay is possible (aqueous photolysis the most likely pathway). Kent Woodburn, personal communication 2005.

Result : Summary (AOP v1.91)

Reaction with N, S and -OH = 0.0000E-12 cm3/moleculoe-sec
Overall OH Rate Constant = 126.5794 E-12 cm3/moleucle-sec
Half-life = 0.085 Days (12-hr day; 1.5E6 OH/cm3)

Summary (AOPv1/91): Ozone Reaction
Overall Ozone Rate Constant = 40 E-17 cm3/molecule-sec
Half-life = 0.029 Days (at 7E11 mol/cm3)

19.12.2005 (3)

3.1.2 STABILITY IN WATER

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level III
Media	:	
Air	:	% (Fugacity Model Level I)
Water	:	% (Fugacity Model Level I)
Soil	:	% (Fugacity Model Level I)
Biota	:	% (Fugacity Model Level II/III)

Soil : % (Fugacity Model Level II/III)
Method : other:calculated
Year :

Method : Level III Fugacity Model; July 2004. Level III model version 2.80.1. Obtained from the Canadian Environmental Modeling Centre, Trent University, Peterborough, Ontario, Canada.
Attached document : Diene 221.doc
Conclusion : This substance has a predicted moderate vapor pressure and low water solubility, is readily biodegradable, has a predicted high reactivity in air, and adsorbs readily to soil/sediment surfaces due to its elevated lipophilicity (i.e., high Kow). If released to water, the compound will be fairly evenly distributed between water and sediment and should undergo primary biodegradation rapidly. If released to soil, virtually the entire mass of chemical will remain in soil, where it will also undergo primary biodegradation very rapidly. If released to air, the compound will remain largely in air and undergo rapid degradation through reaction with hydroxyl radicals and ozone. Finally, if released to all three compartments equally, a majority will be associated with soil and the remainder fairly well distributed between water sediment. In each case, the ubiquitous nature of esterases will produce rapid primary biodegradation of the molecule. Personal communication Kent Woodburn 2005.
Reliability : (2) valid with restrictions
(2): Valid with restrictions: Accepted calculation method. Klimish rating. Klimish HJ et al, Regulatory Toxicology and Pharmacology 1997; 25:1-5.

19.12.2005 (4)

METHOD
Test: Predicted transport between environmental compartments
Method: Level III Fugacity Model
Year: July 2004
Remarks: Level III model version 2.80.1. Obtained from the Canadian Environmental Modeling Centre, Trent University, Peterborough, Ontario, Canada [1].

Input Parameters for Level III Model:

Property	Value	Source
Data Temperature (°C)	25	Default environmental temperature
Chemical Type	1	Type 1 indicates chemical can partition into all environmental compartments
Molecular Mass (g/mol)	220.3	Calculated from molecular structure
Water Solubility (g/m^3)	1.94	Calculated via WSKOWWIN [2]
Vapor Pressure @ 25°C (Pa)	0.17	Calculated via MPBPVP [2]
Melting Point (°C)	47	Calculated via MPBPVP [2]
Henry's Law Constant (Pa*m^3/mole)	0.86	Calculated via HENRYWIN [2]
Log K_{ow} (Octanol-Water Partition Coefficient)	4.97	Calculated via KOWWIN [2]
Simulated Emission Rate (kg/hr)	1,000	Level III Default Values [1]
Simulated Environment	Default Level III environment [1]	
Reaction Half-lives (hr) Input to Level III Model:		
Air (vapor phase)	0.41	Estimated half-life in air via AOPWIN [2]
Water (no susp. solids)	3,60*	Estimated half-lives in water, soil, and sediment extrapolated from predicted inherent biodegradability [2].
Soil	7,20*	
Sediment	3,240*	
Suspended Sediment	**1.0 x 10^{11}	
Fish	**1.0 x 10^{11}	
Aerosol	**1.0 x 10^{11}	

*Half-lives extrapolated from predicted inherent biodegradability, according to Technical Guidance Document of the European Commission [3]. **Default value used in Level III model when reaction is expected to be negligible in this compartment.

RESULTS
Level III: Predicted distribution among air, water, soil, and sediments

Emission Scenario	Percentage and amount distributed to				Residence Time (days) [without advection in brackets]
	Air	Water	Soil	Sediment	
1,000 kg/hr to Air	86.6% 583 kg	1.4% 9 kg	10.3% 69 kg	<0.1% 11 kg	<0.1 [<0.1]
1,000 kg/hr to Water	<0.1% 144 kg	45.1% 2.5E5 kg	<0.1% 17 kg	54.9% 3.0E5 kg	23 [30]
1,000 kg/hr to Soil	<0.1% 1.2 kg	<0.1% 191 kg	100.0% 1.0E6 kg	<0.1% 233 kg	43 [43[
1,000 kg/hr simultaneously to Air, Water, and Soil	<0.1% 729 kg	15.6% 2.5E5 kg	65.3% 1.0E6 kg	19% 3.0E5 kg	22 [24]

Highlighted scenario indicates most probable emission route, based on physical properties and use patterns.

3.3.2 DISTRIBUTION

Media :
Method : Calculation according Mackay, Level I
Year :

Method : Prediction of Equilibrium Environmental Distribution
Method: Level I Fugacity Model, Version 3.00
Year: September 2004
Remarks: Level I model version 3.00, Obtained from the Canadian Environmental Modeling Centre, Trent University, Peterborough, Ontario, Canada.

Attached document : Diene 221 Fugacity Level I.doc

Conclusion : This substance has a low predicted water solubility, moderate vapor pressure, and high log Kow.; the substance therefore has a high potential for adsorption to soil or sediments. In the absence of advective and reactive processes, these physical properties dictate that the substance will be largely distributed to the soil compartment at equilibrium.

Reliability : (2) valid with restrictions
(2): Valid with restrictions: Accepted calculation method. Klimish rating. Klimish HJ et al, Regulatory Toxicology and Pharmacology 1997; 25:1-5.

19.12.2005 (5)

Property	Value	Source
Data Temperature (°C)	25	Default environmental temperature
Chemical Type	1	Type 1 indicates chemical can partition into all environmental compartments
Molecular Mass (g/mol)	220.3	Calculated from molecular structure
Water Solubility (g/m^3)	1.94	Calculated via WSKOWWIN [2]
Vapor Pressure @ 25°C (Pa)	0.17	Calculated via MPBPVP [2]
Melting Point (°C)	47	Calculated via MPBPVP [2]
Henry's Law Constant ($Pa*m^3/mole$)	0.86	Calculated via HENRYWIN [2]
Log K_{ow} (Octanol-Water Partition Coefficient)	4.97	Calculated via KOWWIN [2]
Simulated Emission (kg)	100,000	Level I Default Value [1]
Simulated Environment	Default Level I environment [1]	

RESULTS

Level I: Predicted equilibrium distribution among air, water, soil, and sediments

Emission Scenario	Percentage and amount distributed to			
	Air	Water	Soil	Sediment
100,000 kg total emissions	0.5 % 532 kg	1.16 % 1163 kg	96.1 % 96098 kg	2.1 % 2135 kg

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Contact time	:	
Degradation	:	(±) % after
Result	:	other
Deg. product	:	
Method	:	other:BIOWin
Year	:	
GLP	:	
Test substance	:	

Remark : Personal communication - Kent Woodburn (2005): Should be readily biodegradable and BIOWIN modeling supports this assumption.

19.12.2005

3.6 BOD5, COD OR BOD5/COD RATIO

BOD5		
Method	:	other:calculated
Year	:	
Concentration	:	related to
BOD5	:	mg/l
GLP	:	
COD		
Method	:	other:calculated
Year	:	
COD	:	mg/g substance
GLP	:	

Remark : Personal communication - Kent Woodburn (2005): Should be readily biodegradable and BIOWIN modeling supports this assumption.

19.12.2005

3.7 BIOACCUMULATION

Elimination	:	
Method	:	other
Year	:	
GLP	:	
Test substance	:	

Remark : Personal communication - Kent Woodburn (2005): While the high estimated log Kow value of approximately 5 indicates a potential for bioaccumulation, the instability of the compound in water/soil/sediment will produce as the major metabolite the carboxylic acid, which is highly water soluble and will not pose a bioaccumulation hazard.

Should undergo metabolism via esterases to the corresponding carboxylic acid.

19.12.2005

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	other:Estimated
Species	:	other:freshwater fish
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	ca. .859 calculated
Method	:	other:ECOSAR
Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4

02.12.2005 (6)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	other:estimated
Species	:	Daphnia sp. (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	ca. .347 calculated
Method	:	other:ECOSAR
Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4

02.12.2005 (6)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	other algae:green alga
Endpoint	:	growth rate
Exposure period	:	96 hour(s)
Unit	:	mg/l
EC50	:	ca. .076 calculated
Method	:	other:ECOSAR
Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4

05.12.2005 (6)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 2386 - 1363 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	5
Vehicle	:	other: undiluted
Doses	:	Male: 1000, 2000, 4000 and 8000 mg/kg Female: 1000, 1400 and 2000 mg/kg
Method	:	other:essentially followed OECD guideline 420 fixed doses
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Rats ranging from 200 - 300 grams in weight were used in this study. Five male or female rats per dose level were administered the undiluted test material via stomach intubation. The rats were maintained on appropiate commercial diet and municipal water. Both are available ad libitum except during periods of fasting. Dosage levels for the toxicity test normally doffer by a factor of 2 in a geometric series, but may differ by other constant factors if required. The maximum dosage for the peroral test is 16 ml/kg. Doses are reduced until significant signs of toxicity are not observed. LD50's and the estimated LD50 slopes are calculated by the moving average method (Thompson W, Bact. Rev., 11:115-141 1947; Weil, 1983) and are based on a 14-day observation period. Animal weights are recorded at 0 days (before dose), 7 days and 14 days (just prior to sacrifice). At death or sacrifice, each animal is subjected to gross pathologic evaluation.
Result	:	Signs of toxicity included sluggishness, lacrimation, prostration, kyphosis (in 2), red cruast on perinasal fur and emaciation (in one). Deaths occurred at one to 2 days. Most survivors recovered at one to 5 days. One female recovered at 11 days. Animals that died had pink to red lungs at necropsy. Survivors had no remarkable lesions.
Test substance	:	Clear, colorless non-viscous liquid Percent composition >98%
Conclusion	:	LD50 males = 2386 mg/kg LD50 females = 1363 mg/kg The toxicity terminology used indicated that the LD50 is an extremely low order.
Reliability	:	(1) valid without restriction 1d: Meets generally accepted scientific standards and is described in sufficient detail. Klimish rating. Klimish HJ et al, Regulatory Toxicology and Pharmacology 1997; 25:1-5.

16.12.2005 (7)

Type	:	LD50
Value	:	= 2836 mg/kg bw

Species	:	rat
Strain	:	other: Carworth Farms-Elias
Sex	:	male
Number of animals	:	5
Vehicle	:	other: undiluted
Doses	:	2000, 4000, 8000 mg/kg bw
Method	:	other:essentially followed OECD guideline 420 fixed doses
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Method : Five to six week old rats ranging from 90-120 grams in weight were dosed at levels differing by a factor of 2.0 in a geometric series. The rats were reared in the labs own colony and maintained from time of weaning on Rockland rat diet (complete). The method of moving average for calculating the median-effective dose (LD50) was applied to the 14-day mortality data.

Five male rats per dose level were administered the undiluted test material by stomach tube.

Result : All rats at the 8000 mg/kg group died by day 1; 4 rats at the 4000 mg/kg level died by day 2; and 1 rat at the 2000 mg/kg level died by day 1.

Deaths at the highest dose level occurred within four hours after dosing and were preceded by a narcotic-like stae whild other fatalities were delayed from 24 to 48 hours. Autopsy revealed congestion throughout the lungs and the abdominal viscera.

Test substance : Lot identification - 384RD35

16.12.2005 (8)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	5
Vehicle	:	
Doses	:	
Exposure time	:	6 hour(s)
Method	:	other:essentially followed OECD guideline 403 Acute Inhalation Toxicity
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Method : Five rats per sex weighing between 200 and 300 grams were tested. Essentially saturated test material vapor was produced by passing air (at 2.5 liters/min) through the sample and then through a 9-liter animal chamber (dynamic airflow conditions).

The vapor is produced by enclosing the test material in a sealed 120-liter animal chamber by passing air (at 2.5 liters/min) through the sample and then through a 9-liter animal chamber (dynamic conditions). The chamber oxygen content is mainitained at approximately 20%.

The rats were maintained on appropiate commercial diet and municipal water. Both are available ad libitum except during periods of manipulation. Dosage levels for the toxicity test normally doffer by a factor of 2 in a geometric series, but may differ by other constant factors if required.

Doses are reduced until significant signs of toxicity are not observed.

LD50's and the estimated LD50 slopes are calculated by the moving average method (Thompson W, Bact. Rev., 11:115-141 1947; Weil, 1983) and are based on a 14-day observation period.

Result : There were no deaths of male or female rats during or following the 6-hour test. There were no signs of toxicity or unusual gross pathology observations in either sex.

Test substance : Clear, colorless non-viscous liquid
Percent composition >98%

Reliability : (1) valid without restriction
1d: Meets generally accepted scientific standards and is described in sufficient detail. Klimish rating. Klimish HJ et al, Regulatory Toxicology and Pharmacology 1997; 25:1-5.

16.12.2005 (7)

Type : LC50
Value :
Species : rat
Strain : other:CFE
Sex : female
Number of animals : 6
Vehicle :
Doses :
Exposure time : 8 hour(s)
Method : other:method not indicated
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : Concentrated vapor was generated at a temperature of 21C by passing dried air at the rate of 2.5 liters/minute through a fritted glass disc immersed to a depth of at least one inch in 50 ml. of Diene-221.

Remark : The amount of test material used during the 8-hour exposure was not documented in the report.
The LC50 calculation that was used was not documented in the report.

Result : There were no deaths in a range-finding acute inhalation test where 6 female rats were exposed to concentrated vapors at 21 degrees C for 8-hours. The rats gained weight at a subnormal rate during the subsequent two-week observation period. At necropsy on the 14th day, two rats had focal consolidation of the lungs.

Test substance : Lot identification - 384RD35

16.12.2005 (8)

Type : LC50
Value :
Species : rat
Strain : no data
Sex : female
Number of animals : 6
Vehicle :
Doses :
Exposure time : 8 hour(s)
Method : other:method not indicated
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : Concentrated vapor was generated at a high temperature by passing dried air at the rate of 2.5 liters/minute through a fritted glass disc which was submerged in a silicone oil bath that was maintained at a temperature sufficiently high to keep the Diene-221 at approximately 170C. The

ambient air temperature in the 9-liter inhalation chamber averaged about 27C. Diene-221 changed from a colorless liquid to a dark caramel-colored material during the process.

Result : A group of six female rats survived an eight-hour exposure to mist, vapors, and decomposition products atmosphere but three were found dead the following morning. Necropsy revealed lung hemorrhage as the principal cause of death.

Test substance : Lot identification - 384RD35

Reliability : (3) invalid
3b; Invalid Significant metholodological deficiencies. Klimish rating.
Klimish HJ et al, Regulatory Toxicology and Pharmacology 1997; 25:1-5.

This study is considered invalid because there was significant degradation of the material due to a color change during heating (The material changed from a colorless liquid to a dark caramel-colored material). It is therefore unclear what the animals were actually exposed to.

16.12.2005 (8)

Type : LC50
Value : ca.
Species : rat
Strain : no data
Sex :
Number of animals : 6
Vehicle :
Doses :
Exposure time : 4 hour(s)
Method : other:method not indicated
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Concentrated vapor was generated at a high temperature by passing dried air at the rate of 2.5 liters/minute through a fritted glass disc which was submerged in a silicone oil bath that was maintained at a temperature sufficiently high to keep the Diene-221 at approximately 170C. The ambient air temperature in the 9-liter inhalation chamber averaged about 27C. Diene-221 changed from a colorless liquid to a dark caramel-colored material during the process.

Result : A group of 6 rats survived a four-hour inhalation exposure to mist, vapors, and decomposition products atmosphere and gained weight during the subsequent two-week observation period. On necropsy, day 14, two of the six animals had areas of focal lung consolidation.

Test substance : Lot identification - 384RD35

Reliability : (3) invalid
3b; Invalid Significant metholodological deficiencies. Klimish rating.
Klimish HJ et al, Regulatory Toxicology and Pharmacology 1997; 25:1-5.

This study is considered invalid because there was significant degradation of the material due to a color change during heating (The material changed from a colorless liquid to a dark caramel-colored material). It is therefore unclear what the animals were actually exposed to.

16.12.2005 (8)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50
Value : = 12325 - 13427 mg/kg bw
Species : rabbit
Strain : New Zealand white

Sex	:	male/female
Number of animals	:	5
Vehicle	:	
Doses	:	4000 (female), 8000, 11300 and 16000 mg/kg
Method	:	other:essentially followed OECD guideline 402 Acute Dermal Toxicity
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	New Zealand White rabbits (5/sex except the 4.0 ml/kg level which only had 2 females), weighing between 2.0 and 3.0 kg, were subjected to 24 hours of contact with Diene-221 which was retained under impervious sheeting on the clipped, intact skin of the trunk. As necessary for larger doses, gauze was wrapped around the trunk over the sample to prevent leakage. Vetrap Bandaging Tape was wrapped over the impervious sheeting and the rabbit was returned to its cage for the contact period. Doses are varied by adjusting the volume or weight of the test material. After the contact period, excess fluid was removed to diminish ingestion. Observations for skin reaction were made at one hour, 7 days and 14 days after the contact period.
Result	:	Local dermal effects included erythema, edema, ecchymosis (in one), alopecia (in one) and desquamation. Sluggishness, unsteady gait (in two), diarrhea (in one) and emaciation (in one) were among the signs of toxicity observed. Time to death ranged from 3 to 8 days. Survivors recovered at 2 to 4 days. Gross pathologic findings included pink to red lungs, red tracheas, stomachs with black or white foci, one liver with tan discoloration and red fluid in the thoracic cavity (in two).
Test substance	:	Clear colorless non-viscous liquid TK3651
Conclusion	:	LD50 male rabbits = 12325 mg/kg LD50 female rabbits = 13427 mg/kg
Reliability	:	(1) valid without restriction 1d: Meets generally accepted scientific standards and is described in sufficient detail. Klimish rating. Klimish HJ et al, Regulatory Toxicology and Pharmacology 1997; 25:1-5.

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Type	:	LD50
Value	:	= 5010 mg/kg bw
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	male
Number of animals	:	8
Vehicle	:	other:undiluted
Doses	:	5010 and 10000 mg/kg
Method	:	other:essentially followed OECD guideline 402 Acute Dermal Toxicity
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Eight male albino New Zealand rabbits, three to five months of age and averaging 2.5 kg were immobilized during the 24-hour contact period. The doses were 5,000 and 10,000 mg/kg. Thereafter, the polyethylene sheeting used to retain the dose in contact with the clipped skin of the trunk was removed and the animals were caged for the remainder of the 14-day observation period. The moving average method of calculating the LD50 was used.
Result	:	Deaths occurred from three to six days after application of Diene 221. For the high dose animals 2 died at 3 days; one died at four days; and one died at five days. For the 5000 mg/kg dose group one died at five days and one died at six days. The remaind two live until study termination. Gross necropsy disclosed some lung congestion, dark mottled livers with acini

prominent, and pale mottled kidneys. The urine of two rabbits contained what appeared to be blood.

Test substance : Lot identification - 384RD35

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5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Occlusive
Exposure time	:	4 hour(s)
Number of animals	:	6
Vehicle	:	other:undiluted
PDII	:	
Result	:	slightly irritating
Classification	:	
Method	:	other:essentially followed OECD 404 Acute Dermal Irritation
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Method : Male or female New Zealand white rabbits were dosed with 0.5 ml. The dose was applied to the clipped, intact skin under a gauze patch and was loosely covered with impervious sheeting. Diene-221 was applied to each of 6 rabbits, which were restarined for the 4-hour contact period. Excess sample was removed after contact. Skin reaction was scored, by the Draize method, at one hour, one day, 2 days, 3 days, and 7 days.

Result : Minor erythema 1/6 and minor edema 4/6. After 2 days, no irritation was present. Desquamation appeared on 5/6 after 7 days, but no other reaction was apparent.

Test substance : Clear, colorless non-viscous liquid
Percent composition >98%

Reliability : (1) valid without restriction
1d: Meets generally accepted scientific standards and is described in sufficient detail. Klimish rating. Klimish HJ et al, Regulatory Toxicology and Pharmacology 1997; 25:1-5.

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Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Open
Exposure time	:	no data
Number of animals	:	5
Vehicle	:	other:none
PDII	:	
Result	:	slightly irritating
Classification	:	
Method	:	other:method not indicated
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Remark : No information on method

Result : Uncovered application of 0.01 ml amounts of Diene-221 to the clipped skin of the rabbit belly resulted in no reation on four animals and marked capillary injection on a fifth. Grade 2 in a 10 grade rating system.

Test substance	:	Lot identification - 384RD35
Reliability	:	(3) invalid 3b; Invalid Significant metholodological deficiencies. Klimish rating. Klimish HJ et al, Regulatory Toxicology and Pharmacology 1997; 25:1-5. This study is considered invalid because the liquid was applied without a gauze patch to the skin. Access by the animal to the test material was not prevented. Also accoring to the OECD guideline 404 a 0.5 ml of test material should be applied. Only 0.01 ml was applied. It is therefore unclear what the animals were actually exposed to.

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5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure time	:	
Comment	:	no data
Number of animals	:	6
Vehicle	:	none
Result	:	slightly irritating
Classification	:	irritating
Method	:	other:essentially followed OECD 405 Acute Eye Irritation
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The dose is instilled into the lower conjunctival sac of one eye per animal. The eyelids are held together for one second. Six eyes are dosed per test volume. The eyes are scored at one hour, approximately 4 hours, one day, 2 days, 3 days and 7 days post-dosing. Fluorescein (2%) staining was used to determine corneal injury before dosing and at readings after one day.
Result	:	Instillation of 0.1 ml of test material into rabbit eyes resulted in no corneal injury or iritis in any of the 6 animals. Minor conjuctival irritation developed in 4 rabbits and all eyes exhibited substantial ocular discharge. By 24 hours, 3 eyes had a normal appearance. One eye still had minor conjuctival redness and 2 had slight discharge. All 6 eyes were healed at 48 hours. Observations continued for 7 days after treatment.
Test substance	:	Clear, colorless non-viscous liquid Percent composition >98%
Reliability	:	(1) valid without restriction 1d: Meets generally accepted scientific standards and is described in sufficient detail. Klimish rating. Klimish HJ et al, Regulatory Toxicology and Pharmacology 1997; 25:1-5.

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Species	:	rabbit
Concentration	:	undiluted
Dose	:	.5 ml
Exposure time	:	
Comment	:	
Number of animals	:	4
Vehicle	:	none
Result	:	
Classification	:	
Method	:	other:method not indicated
Year	:	
GLP	:	no data

Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Method not indicated, however, the method may have followed that described in the article by Carpenter and Smyth, "Chemical Burns of the Rabbit Cornea", American Journal of Opthalmology, 1947.
Result	:	Four rabbit eyes were apparently unharmed and a fifth suffered only trace injuries following the instillation of an excess (0.5 ml) of the undiluted chemical. Grade 1 in a 10 grade rating system. There were no corneal injuries.
Reliability	:	(3) invalid 3b; Invalid Significant metholodological deficiencies. Klimish rating. Klimish HJ et al, Regulatory Toxicology and Pharmacology 1997; 25:1-5. This study is considered invalid because as per the OECD guideline 0.1 ml is stated amount of test material to instill into the eye. This study instilled 0.5 ml.

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5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

5.5 GENETIC TOXICITY 'IN VITRO'

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

(1) U.S. EPA. (2004). EPI Suite software, version v3.12. United States Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, D. C. Available at: http://www.epa.gov/oppt/exposure/docs/episuitedl.htm

(2) U.S. EPA, 2004. EPI Suite software, version v3.12. United States Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, D.C. Available at: http://www.epa.gov/oppt/exposure/docs/episuitedl.htm

(3) U.S. EPA, 2000. - AOP v1.90, Atmospheric half-life estimating software & experimental value database.

(4) Mackay, D., 2001. Multimedia Environmental Models: The Fugacity Approach. Lewis Publishers, CRC Press, Boca Raton, FL. Models available at: http://www.trentu.ca/cemc/models.html\

(5) Mackay, D., 2001. Multimedia Environmental Models: The Fugacity Approach. Lewis Publishers, CRC Press, Boca Raton, FL. Models available at: http://www.trentu.ca/cemc/models.html

(6) Cash G and Nabholz V 2001. U.S. EPA OPPT - ECOSAR, v0.99g, Aquatic organism toxicity estimating software for the class of esters.

(7) Myers RC, Slesinski RS and Frank FR (1987). Diene 221 (Cyclohex-3-enylmethyl-3-cyclohexencarboxylate) Acute Toxicity and Primary Irritancy Studies, Unpublished report of the Union Carbide Corporation.

(8) Striegel JA and Carpenter CP (1961) Range Finding Tests of Diene-221. Mellon Institute of Industrial Research, Pittsburgh, PA. Unpublished report 24-93 of the Union Carbide Corporation.

10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT